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(71) Applicant *(for all designated States except US)*: EIDGENOESSISCHE TECHNISCHE HOCHSCHULE ZUERICH [CH/CH]; Rämistrasse 101, CH-8092 Zürich (CH).

(72) Inventor; and

(75) Inventor/Applicant *(for US only)*: ZAHN, Ralph [DE/CH]; Michelstr. 13, CH-8049 Zürich (CH).

(74) Agent: HEUSCH, Christian; OK pat AG, Chamerstrasse 50, CH-6300 Zug (CH).

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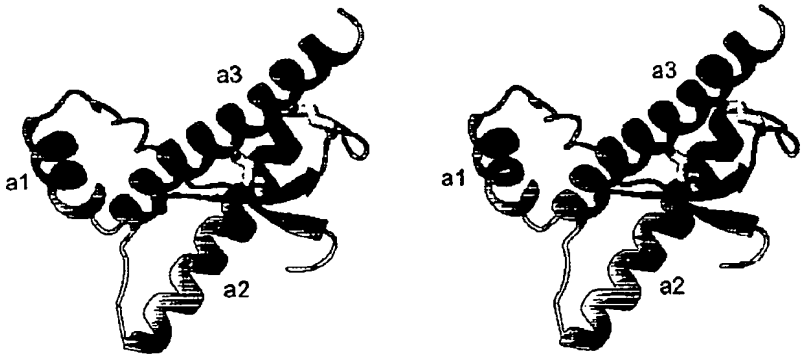
(54) Title: MUTANT PROTEINS AND USE THEREOF FOR THE MANUFACTURE OF MEDICAMENTS AND THE TREATMENT OF HUMANS OR ANIMALS SUFFERING FROM CONFORMATIONAL DISEASES



(57) Abstract: The invention relates to a mutant prion protein (PrP), the globular domain of which comprises an engineered second disulfide bond in a similar position as in the human doppel protein (hDpl). In an embodiment, the prion protein has an engineered extra disulfide bond in the presumed 'factor X' binding epitope and is accommodated with slight, strictly localized conformational changes to inhibit prion propagation in human and animals. Also disclosed is the use of a mutant prion protein (PrP), the globular domain of which comprises at least one engineered additional disulfide bond in a similar position as in the human doppel protein, or fragments thereof for therapeutic treatment or for the manufacture of a medicament for therapeutic treatment of proteins causing disease after a conformational transition, e.g. Transmissible Spongiform Encephalopathy (TSE), variant forms of Creutzfeldt-Jakob disease (CJD), fatal familial insomnia (FFI), and Gerstmann-Sträussler-Scheinker syndrome (GSS) in human. Further, the use of the PrP mutant protein for in vivo generation of disulfide mutants of prion proteins or fragments thereof is carried out in order to enable an intended ther-apy of TSE in animals, e.g. by somatic gene therapy with lentiviral vector, where TSE includes bovine spongiform encephalopathy (BSE), scrapie in sheep, feline spongiform encephalopathy (FSE), and chronic wasting disease (CWD) in elk and deer.

WO 2004/007546 A1